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## PF-0456-2 DIV

## What is claimed is:

- 1. An isolated polypeptide selected from the group consisting of:
- a) a polypeptide comprising an amino acid sequence of SEQ ID NO:1 or SEQ ID NO:3,
- b) a naturally occurring polypeptide comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1 or SEQ ID NO:3,
- c) a biologically active fragment of a polypeptide having the amino acid sequence of SEQ ID NO:1 or SEQ ID NO:3, and
- d) an immunogenic fragment of a polypeptide having the amino acid sequence of SEQ ID NO:1 or SEQ ID NO:3.
  - 2 An isolated polypeptide of claim 1 selected from the group consisting of SEQ ID NO:1 and SEQ ID NO:3.
    - 3. An isolated polynucleotide encoding a polypeptide of claim 1.
    - 4. An isolated polynucleotide encoding a polypeptide of claim 2.
  - 5. An isolated polynucleotide of claim 4 selected from the group consisting of SEQ ID NO: 2 and SEQ ID NO:4.
  - 6. A recombinant polynucleotide comprising a promoter sequence operably linked to a polynucleotide of claim 3.
    - 7. A cell transformed with a recombinant polynucle tide of claim 6.
    - 8. A transgenic organism comprising a recombinant polynucleotide of claim 6.
    - 9. A method for producing a polypeptide of claim 1, the method comprising:
- a) culturing a cell under conditions suitable for expression of the polypeptide, wherein said cell is transformed with a recombinant polynucleotide, and said recombinant polynucleotide comprises a promoter sequence operably linked to a polynucleotide encoding the polypeptide of claim 1, and



- b) recovering the polypeptide so expressed.
- 10. An isolated antibody which specifically binds to a polypeptide of claim 1.

11. An isolated polynucleotide selected from the group consisting of:

a) a polynucleotide comprising a polynucleotide sequence of SEQ ID NO:2 or SEQ ID

NO:4,

b) a naturally occurring polynucleotide comprising a polynucleotide sequence at least 90% identical to the polynucleotide sequence of SEQ ID NO:2 or SEQ ID NO:4,

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- c) a polynucleotide complementary to a polynucleotide of a),
- d) a polynucleotide complementary to a polynucleotide of b), and
- e) an RNA equivalent of a)-d).

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12. An isolated polynucleotide comprising at least 60 contiguous nucleotides of a polynucleotide of claim 11.

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- 13. A method for detecting a target polynucleotide in a sample, said target polynucleotide having a sequence of a polynucleotide of claim 11, the method comprising:
- a) hybridizing the sample with a probe comprising at least 20 contiguous nucleotides comprising a sequence complementary to said target polynucleotide in the sample, and which probe specifically hybridizes to said target polynucleotide, under conditions whereby a hybridization complex is formed between said probe and said target polynucleotide or fragments thereof, and
- b) detecting the presence or absence of said hybridization complex, and, optionally, if present, the amount thereof.

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- 14. A method of claim 13, wherein the probe comprises at least 60 contiguous nucleotides.
- 15. A method for detecting a target polynucleotide in a sample, said target polynucleotide having a sequence of a polynucleotide of claim 11, the method comprising:

- a) amplifying said target polynucleotide or fragment thereof using polymerase chain reaction amplification, and
- b) detecting the presence or absence of said amplified target polynucleotide or fragment thereof, and, optionally, if present, the amount thereof.

- 16. A composition comprising a polypeptide of claim 1 and a pharmaceutically acceptable excipient.
- 5 17. A composition of claim 16, wherein the polypeptide has an amino acid sequence of SEQ ID NO:1 or SEQ ID NO:3..
  - 18. A method for treating a disease or condition associated with decreased expression of functional HMRP, comprising administering to a patient in need of such treatment the composition of claim 16.
  - 19. A method for screening a compound for effectiveness as an agonist of a polypeptide of claim 1, the method comprising:
    - a) exposing a sample comprising a polypeptide of claim 1 to a compound, and
    - b) detecting agonist activity in the sample
  - 20. A composition comprising an agonist compound identified by a method of claim 19 and a pharmaceutically acceptable excipient.
  - 21. A method for treating a disease or condition associated with decreased expression of functional HMRP, comprising administering to a patient in need of such treatment a composition of claim 20.
- 22. A method for screening a compound for effectiveness as an antagonist of a polypeptide of claim 1, the method comprising:
  - -a)-exposing-a-sample-comprising-a-polypeptide-of-claim-1-to-a-compound, and
  - b) detecting antagonist activity in the sample.
- 23. A composition comprising an antagonist compound identified by a method of claim 22 and a pharmaceutically acceptable excipient.
  - 24. A method for treating a disease or condition associated with overexpression of functional HMRP, comprising administering to a patient in need of such treatment a composition of

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- 25. A method of screening for a compound that specifically binds to the polypeptide of claim 1, said method comprising the steps of:
- a) combining the polypeptide of claim 1 with at least one test compound under suitable conditions, and
- b) detecting binding of the polypeptide of claim 1 to the test compound, thereby identifying a compound that specifically binds to the polypeptide of claim 1.
- 26. A method of screening for a compound that modulates the activity of the polypeptide of claim 1, said method comprising:
- a) combining the polypeptide of claim 1 with at least one test compound under conditions permissive for the activity of the polypeptide of claim 1,
- b) assessing the activity of the polypeptide of claim 1 in the presence of the test compound, and
- c) comparing the activity of the polypeptide of claim 1 in the presence of the test compound with the activity of the polypeptide of claim 1 in the absence of the test compound, wherein a change in the activity of the polypeptide of claim 1 in the presence of the test compound is indicative of a compound that modulates the activity of the polypeptide of claim 1.
- 27. A method for screening a compound for effectiveness in altering expression of a target polynucleotide, wherein said target polynucleotide comprises a sequence of claim 5, the method comprising:
- a) exposing a sample comprising the target polynucleotide to a compound, under conditions suitable for the expression of the target polynucleotide,
  - \_b)\_detecting altered\_expression\_of\_the\_target\_polynucleotide,\_and
- c) comparing the expression of the target polynucleotide in the presence of varying amounts of the compound and in the absence of the compound.
  - 28. A method for assessing toxicity of a test compound, said method comprising:
  - a) treating a biological sample containing nucleic acids with the test compound;
- b) hybridizing the nucleic acids of the treated biological sample with a probe comprising at least 20 contiguous nucleotides of a polynucleotide of claim 11 under conditions whereby a specific

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hybridization complex is formed between said probe and a target polynucleotide in the biological sample, said target polynucleotide comprising a polynucleotide sequence of a polynucleotide of claim 11 or fragment thereof;

- c) quantifying the amount of hybridization complex; and
- d) comparing the amount of hybridization complex in the treated biological sample with the amount of hybridization complex in an untreated biological sample, wherein a difference in the amount of hybridization complex in the treated biological sample is indicative of toxicity of the test compound.
- 29. A diagnostic test for a condition or disease associated with the expression of HMRP in a biological sample comprising the steps of:
  - a) combining the biological sample with an antibody of claim 10, under conditions suitable for the antibody to bind the polypeptide and form an antibody:polypeptide complex; and
  - b) detecting the complex, wherein the presence of the complex correlates with the presence of the polypeptide in the biological sample.
    - 30. The antibody of claim 10, wherein the antibody is:
    - a) a chimeric antibody,
    - b) a single chain antibody,
    - c) a Fab fragment,
    - d) a F(ab'), fragment, or
    - e) a humanized antibody.
    - 31. A composition comprising an antibody of claim 10 and an acceptable excipient.
  - 32. A method of diagnosing a condition or disease associated with the expression of HMRP in a subject, comprising administering to said subject an effective amount of the composition of claim-31.
    - 33. A composition of claim 31, wherein the antibody is labeled.
  - 34. A method of diagnosing a condition or disease associated with the expression of HMRP in a subject, comprising administering to said subject an effective amount of the composition of claim 33.

35. A method of preparing a polyclonal antibody with the specificity of the antibody of claim 10 comprising:

- a) immunizing an animal with a polypeptide having an amino acid sequence of SEQ ID NO:1 or SEQ ID NO:3,, or an immunogenic fragment thereof, under conditions to elicit an antibody response;
  - b) isolating antibodies from said animal, and
- c) screening the isolated antibodies with the polypeptide, thereby identifying a polyclonal antibody which binds specifically to a polypeptide having an amino acid sequence of SEQ ID NO:1 or SEQ ID NO:3.

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- 36. An antibody produced by a method of claim 35.
- 37. A composition comprising the antibody of claim 36 and a suitable carrier.
- 38. A method of making a monoclonal antibody with the specificity of the antibody of claim 10 comprising:
- a) immunizing an animal with a polypeptide having an amino acid sequence of SEQ ID NO:1 or SEQ ID NO:3, or an immunogenic fragment thereof, under conditions to elicit an antibody response;
  - b) isolating antibody producing cells from the animal;
- c) fusing the antibody producing cells with immortalized cells to form monoclonal antibody-producing hybridoma cells;
  - d) culturing the hybridoma cells, and
- e) isolating from the culture monoclonal antibody which binds specifically to a polypeptide having an amino acid sequence of SEQ ID NO:1 or SEQ ID NO:3..
  - 39. A monoclonal antibody produced by a method of claim 38.
  - 40. A composition comprising the antibody of claim 39 and a suitable carrier.

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- 41. The antibody of claim 10, wherein the antibody is produced by screening a Fab expression library.
- 42. The antibody of claim 10, wherein the antibody is produced by screening a recombinant immunoglobulin library.

- 43. A method for detecting a polypeptide having an amino acid sequence of SEQ ID NO:1 or SEQ ID NO:3 in a sample, comprising the steps of:
- a) incubating the antibody of claim 10 with a sample under conditions to allow specific binding of the antibody and the polypeptide; and
- b) detecting specific binding, wherein specific binding indicates the presence of a polypeptide having an amino acid sequence of SEQ ID NO:1 or SEQ ID NO:3 in the sample.
- 44. A method of purifying a polypeptide having an amino acid sequence of SEQ ID NO:1 or SEQ ID NO:3 from a sample, the method comprising:
- a) incubating the antibody of claim 10 with a sample under conditions to allow specific binding of the antibody and the polypeptide; and
- b) separating the antibody from the sample and obtaining the purified polypeptide having an amino acid sequence of SEQ ID NO:1 or SEQ ID NO:3.
  - 45. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:1.
  - 46. A polypeptide of claim 1, comprising the amino acid sequence of SEQ ID NO:3
  - 47. A polynucleotide of claim 11 comprising the polynucleotide sequence of SEQ ID
- 48. A polynucleotide of claim 11, comprising the polynucleotide sequence of SEQ ID NO:4.

NO:2.

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